

ON THE ORIGIN OF CANCER.

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IN discussing such a question as the Origin of Cancer, in a short paper like the present, it is absolutely necessary to take some propositions for granted, since it is impossible to subject every statement which can be made with regard to the origin of the disease to rigid analysis. It will be generally conceded that cancer is neither propagated by contagion, nor by inoculation; and that it is probably never developed in a healthy individual by continued irritation, unless there is an inherited tendency to the growth of the disease, or of its allies. The truth of these propositions will, at any rate, be taken for granted here. The object of the present paper is to show that cancer may have been developed from innocent epithelial growths, by continued irritation acting upon these growths as they appear in a succession of individuals, and causing them to deviate further and further from healthy tissues. It is evident that every deviation produced must be of such a nature as to become inherited, otherwise it would be impossible to get an accumulated action in a succession of individuals. Suppose, for instance, that an individual has a small growth (A), which by irritation becomes (A + R), it is manifest that if neither (A) nor (A + R) reappear in the offspring, no accumulation of results is possible. Even if (A) alone is bequeathed to the offspring, it would only become (A + R) under the irritation supposed, and the result in a succession of organisms would still not be cumulative. But if both (A) and (R) are inherited, the growth (A + R) would tend to appear in the offspring at a certain age, and this, by continued irritation, might become (A + 2 R); and, if the latter were transmitted, it would, under similar circumstances of irritation in the next generation, become (A + 3 R); and so on

indefinitely. In tracing, therefore, the genesis of cancer from the simple epithelial growths, which can be cultivated upon a healthy individual by changes in the incident forces, it is essential that every increment of deviation (represented by the (R) in the foregoing formulæ) should be of such a nature as to insure its own reappearance by inheritance. But all the structural changes which it is possible for an irritant to produce in an innocent epithelial growth are not inherited; hence we must endeavour to draw a distinction between the structural changes which *are*, and those which *are not* transmitted to posterity. To enable us to make such a distinction, it is necessary to notice very briefly the general laws of inheritance.

On taking a wide glance at all the peculiarities which are inherited, we find that each must bear a constant and definite relation to the structure of the individual as a whole, and more especially to the structure of the immediately correlated parts of the organism. The same idea may be expressed in terms of function, by saying that the functional activity of a peculiarity which tends to be inherited, must be in equilibrium with the functional activities of all the parts of the body; and especially with those of the parts which are more immediately correlated with it. Let us now briefly apply this rule to the explanation of the phenomena of inheritance. The structural peculiarities which characterise the species (biological), and the variety, must be in equilibrium with one another, and with the structure of the individual as a whole; since the individuals whose organs are not in equilibrium with one another would be eliminated by natural selection. If one organ of the body is not in equilibrium with the rest, it involves expenditure without equivalent return in function, and the individual will lose in the struggle for existence. But as the species and the variety are groups of individuals which have remained stable for comparatively long periods, it follows that all the peculiarities which characterise them must be in equilibrium with one another, and that, in accordance with our rule, they will reappear in the offspring, unless counteracted by other causes. This is also true, although to a more limited extent, with regard to the structural peculiarities which characterise the family. It is noticeable that a congenital

peculiarity always exhibits a strong tendency to become inherited. The reason is that a congenital deviation is already in equilibrium with the aggregate functions of the organism ; and its first appearance is a result, and not a cause, of this equilibrium. But functionally acquired peculiarities, and it is with such that we have mainly to do here, must generally act upon the organism at large for a long time, so as to bring about the correlative changes necessary to form a new equilibrium, otherwise they will fail to be inherited. If a part of the body becomes altered in size, owing to changed incident forces, the nerves and blood-vessels leading to it must undergo corresponding changes, and secondary changes must occur in the more remote parts of the organism ; and it is not until these reverberate throughout the entire system that a stable equilibrium is formed, which will ensure the transmission of the primary deviation to the progeny. It is thus that the callosities which form on the hands of gentlemen by rowing, being of a transient character, are not inherited ; while the large hands of agricultural labourers, having arisen from incident forces which have acted for long periods of time, are transmitted. But even the latter disappear in a few generations, when the incident forces which have originally caused the peculiarity cease to act. This is well exemplified in the case of the descendants of agricultural labourers who now work in our cotton factories. But the rule, that the incident forces which have produced an inherited functional peculiarity must act upon the organism for a long time, has some important exceptions. Dr. Brown Séquard has found that epilepsy can be induced in a guinea pig by section of one-half of the spinal cord ; and that the subsequent progeny of the injured animals are subject to epileptic attacks. Here, then, is an instance where the functionally acquired peculiarity is produced by a stroke of a knife, and yet it is found to be inherited. But it must be remembered that the epilepsy is only a secondary result of the primary injury, and that neither the injury itself, nor the paralysis which directly results from it, is inherited. The injury has affected an important structure, which has a wide and intimate connection with almost every part of the body, and a tissue so highly specialised as to be able

to affect every part of the organism almost simultaneously; hence the functions and structure of such a large portion of the body are so disturbed that the parts which remain more or less healthy are never afterwards able to regain the equilibrium which existed prior to the injury, and a certain nervous susceptibility remains permanent in the individual which develops an epileptic attack upon slight external causes.

We have seen that there are two classes of functional peculiarities which tend to be inherited, and that the equilibrium which ensures their transmission is brought about, in the one by the long continued action of altered external forces, and in the other, almost immediately, by a profound disturbance of a wide tract of tissue; and if we can now only find some rule or law to which both of these extremes conform, it will probably be applicable to all other cases, and be the very rule which will help us to explain the genesis of cancer from innocent epithelial growths. The rule which is applicable to both cases is, that when a transmissible modification once appears, it must remain permanent during the subsequent life-time of the individual. This rule is not absolutely true. It is a derivative law, which is liable to some exceptions, but it is impossible to specify these at present. In the meantime, no error will arise if we say that a functional peculiarity, which appears for a short time, and then returns to the family likeness, or what may be termed the normal condition, is not inherited. In other words, if the variation is of such a nature that the organism can be readapted to its former equilibrium, it fails to be transmitted. On the other hand, a functional modification, which either remains permanent during the subsequent life of the individual, or which, instead of returning to the normal condition, develops into some other form which becomes permanent, will tend to be inherited. The fact of the modification remaining permanent shows that the aggregate forces of the body have not been able to readapt the part to its former equilibrium, and that the variation is, in accordance with our primary law, in equilibrium with the aggregate functions of the body. In applying this rule to the genesis of cancer from innocent growths, every deviation which occurs in the latter must be of such a nature as to

become permanent during the subsequent life-time of the individual, and must therefore give an additional degree of independence to the growth, as against the aggregate forces of the organism, otherwise the growth will become readapted to its former equilibrium and the deviation will fail to be transmitted.

Cancer may be defined, for practical purposes, as an infectious tumour, whose cells are derivatives from true epithelium. We must, therefore, look for the origin of cancer in the minor deviations from healthy structure of the epithelial tissues of the body. There are three minor structural changes of the skin which are closely allied, and yet present slight divergences, which it is important to notice. These are callosities, corns, and warts. The first and second of these may be produced upon the skin of a healthy individual by prolonging irritation applied in a particular manner. It is probable that the third may also be cultivated upon a healthy skin; but this is more doubtful; and, at any rate, there can be no doubt that a greater complexity of causes is necessary to the production of the latter than of either of the former. But if a greater complexity of causes is necessary for the production of a wart than of a callosity, the former, when once produced, is more independent of the originating causes than the latter. A callosity begins to disappear when the incident forces which caused it cease to act; but a wart frequently maintains itself during the subsequent life of the individual, independently of the causes which first produced it. But this constitutes the outward sign of those functional peculiarities which tend to be inherited; and it is proved by observation, that warts appear more frequently in some families than in others. We must now look more narrowly at the internal differences which exist between a callosity and a wart, with a view of explaining what gives to the latter its power of maintaining its individuality against the aggregate forces of the body; while the former begins to disappear when the incident forces which first produced it are withdrawn.

The most obvious difference between a callosity and a wart is, that while the units of the former are deposited amongst those of

the tissues in which it is developed, the units of the latter are aggregated together, so as to form a continuous growth. The consequence of this difference is, that the aggregate forces of the body will have less power over the wart than over the callosity; hence the structure of the part in which the former grows is not so readily readapted to its former equilibrium as that in which the latter forms. This difference, therefore, slight as it is, makes the wart, when once it is formed, more independent of the aggregate forces of the body than the callosity.

Another difference between a callosity and a wart is, that while the units of the former are arranged in the same structural order as those of the tissue in which it is developed, those of the latter lose almost all structure. But structure entails cost, and the absence of structure is an economy of force in one direction which may be expended in another. The units of a wart, therefore, which have to expend less than those of a callosity in arranging themselves into a definite structure, can expend more in self multiplication and maintenance. This also increases the power of the wart in maintaining its independence against the aggregate forces of the body. The general result, therefore, of the differences which exist between the callosity and the wart is a double gain to the latter. On the one hand, the aggregate forces of the organism act upon it at a disadvantage; while on the other its units have acquired additional powers of self maintenance.

But another element may now come into play, which will greatly increase the molecular forces of the wart. When it is irritated by incident forces, its tissues, like those of any other part of the body, will tend to proliferate, and this will increase its molecular forces. Mr. Herbert Spencer says, "that those extremely active changes which go on during the early stages of evolution, imply an immense excess of the molecular forces over those antagonist forces which the aggregate exercises on the molecules." And this is as true of a local growth as of the entire organism. As the units of a growth proliferate, and its substance becomes more and more like embryonic tissue, the molecular forces which it opposes to the antagonist forces of the organism become

greater; and the tumour itself, within certain limits to be hereafter mentioned, acquires higher powers of self maintenance. This local change in the tumour must, however, be accompanied by correlative changes in the organism at large, in order that the equilibrium which will ensure the transmission of the variation to the offspring may be brought about. We shall now endeavour to trace how each increment of deviation acts upon the organism in such a manner as to produce this equilibrium.

It has already been noticed, that the fact of the units of a wart being aggregated as a continuous growth, and losing all structural development, enables it frequently to maintain its individuality during the subsequent life-time of the individual; and this permanence will of itself tend to bring the aggregate forces of the organism into equilibrium with those of the tumour. Again, the increased powers of multiplication which loss of structural development gives to the units of a growth will enable it frequently, especially if aided by a certain amount of external irritation, to add constantly to its size; and size, other things being equal, will give to the tumour additional powers to modify the organism, and to bequeath a corresponding modification to the offspring. But there is another mode by which a tumour profoundly modifies the organism. When the tissues of a tumour acquire great molecular mobility by cell proliferation, some of its units will enter the circulation, and in this manner traverse the entire organism. We may infer, from deductive reasoning, that such transference of units will take place, and it is rendered certain, by observation, that this transference does actually occur in the more infectious tumours. These units will tend to generate their like throughout the body, and in this manner they will bring the entire organism into equilibrium with the local growth; and this, of course, will ensure the inheritance of the latter. The units distributed throughout the organism will, owing to the special affinities of the tissues, accumulate and form growths at certain *foci*; and the implication is, that, at whatever part of the body the tissues become assimilated to the units of the tumour, the molecular forces which end in growth will be increased, while those which produce active function are diminished

in a corresponding degree. When this assimilation of the tissues of the body to that of the tumour proceeds to a large extent, which it must inevitably do when the molecular mobility of the tumour is great, the forces which produce function will be so diminished that they will only be able to balance the aggregate forces which the organism opposes to them, an unstable equilibrium is formed, and death results.

But although it is true that as the units of a growth acquire higher powers of multiplication, the growth itself will possess greater powers of modifying the organism; yet if it is to become inherited, the multiplication of units must proceed within certain very narrow limits. We have already seen that a growth, to be inherited, must, when once it appears, remain permanent during the subsequent life-time of the individual; but if the cells of the growth multiply very rapidly, it will dissolve into a tissue like pus, with independent units, which will become detached, and consequently the growth will fail to be transmitted. Again, if the units of a growth multiply very rapidly, even if they are able to maintain themselves aggregated as a continuous growth, a great many of them will enter the circulation, and produce a fatal result in such a short time that no progeny can be left to inherit the peculiarity; and this will restrict still further the rate of multiplication of the units of an inherited tumour. An infectious tumour is also limited with regard to the age at which it becomes active. As it is always fatal, if it were to become active before the age of puberty, no progeny would be left to inherit the peculiarity at the same age. Cancer will not, therefore, appear generally till after the age of puberty, except occasionally in childhood, as the result of transmission by direct continuity, when the disease is more or less active in one of the parents. I may mention, in conclusion, without having time to prove, that the endogenous mode of multiplication of the cancerous cells gives to the growth the greatest stability, to render it permanent during the subsequent life-time of the individual; along with the highest molecular mobility, to enable it to infect the organism.